Predictors of wound complications following major amputation for critical limb ischemia

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Objectives: **For patients with end-stage critical limb ischemia (CLI) who have already suffered over an extended period of time, a major amputation that is free of wound complications remains paramount. Utilizing data from the American College of Surgeons, National Surgical Quality Improvement Program (ACS-NSQIP), the objective of this report was to determine critical factors leading to wound complications following major amputation.**

Methods: **ACS-NSQIP was used to identify patients ≥50 years, with CLI, and having an ipsilateral below-(BKA) or above-knee amputation (AKA). The primary outcome was wound occurrence (WO) defined by affirmative findings of superficial infection, deep infection, and/or wound disruption. The secondary outcome was 30-day mortality. Following univariate analyses, a multiple logistic regression was performed to identify predictive factors.**

Results: **Between January 1, 2005 and December 31, 2008, 4250 patients fulfilled inclusion criteria (2309 BKAs and 1941 AKAs). WOs were 10.4% for BKAs and 7.2% for AKAs. For BKAs, increasing elevation in international normalized ratio (INR) predicted more WOs ($P = .008$, odds ratio [OR] 1.5 for every integral increase in INR) as did age 50 to 59 compared with older patients ($P = .002$, OR 1.9). For AKAs, being a current smoker predicted more WOs ($P = .0008$, OR 1.8) as did an increasing body mass index (BMI) ($P = .02$, OR 1.3 for every 10 kg/m^2 increase in BMI). Mortality was 7.6% for BKAs and 12% for AKAs. Complete functional dependence was most predictive of mortality following AKA ($P < .0001$, OR 2.5). Medical comorbidities such as history of myocardial infarction (MI) (OR 1.8), congestive heart failure (CHF, OR 1.6), and chronic obstructive pulmonary disease (COPD, OR 1.6) predicted mortality following BKA, while dialysis use (OR 2.4), CHF (OR 2.3), and COPD (OR 2.1) predicted mortality following AKA.**

Conclusions: **Wound occurrences and mortality rates after major amputation for CLI continue to be a prevalent problem. Normalization of the INR prior to BKA should decrease WOs. Heightened awareness in higher risk patients with improved preventive measures, earlier disease recognition, better treatments, and increased education remain critical to improving outcomes in an already stressed patient cohort. (J Vasc Surg 2011;54:1374-82.)**

The treatment of critical limb ischemia (CLI) from peripheral arterial disease continues to represent a serious challenge for vascular surgeons. For those patients who are not candidates for revascularization or for those whom interventions have failed, 20% to 40% will undergo major amputation within 6 to 12 months.[1,2] Historically, morbidity and mortality following major amputation of the lower extremity in this patient population has been high. Recent studies have cited 30-day mortality rates ranging from 6% to 17%, with greater risk among patients with renal failure, prior coronary revascularization, advanced age, and transfemoral vs transtibial amputation.[3-7]

Despite these aforementioned challenges surrounding amputation for CLI, mainstay goals remain uncomplicated wound healing and, for appropriate candidates, progression to use of a prosthesis for ambulation or transfer. Perioperative wound complications can be devastating in this already debilitated population and can range from 13% to 30%.[3-6] The objective of this investigation was to identify critical factors that predispose to wound complications following major amputation in patients with end-stage CLI.

METHODS

Database. The American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) is a validated process to obtain data for the purposes of improving quality of care.[8] Data for this study were obtained from a systematic sampling of operations performed by general and vascular surgeons in the private sector. There were 121 hospitals (community and academic) enrolling patients at the start of 2005, which increased to 211 hospitals by the end of 2008. Preoperative risk factors, intraoperative variables, and 30-day postoperative morbidity and mortality data are collected, validated, and reported back to participating hospitals. Outcomes for each hospital are benchmarked to each other to identify key areas for improvement. Additionally, the entire database or parts of it can be made available in a blinded fashion after an application process to answer specific research questions from all participating hospitals. The ACS-NSQIP and the hospitals participating in the ACS-NSQIP are the source of data used herein, and they have not verified and are not

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Table I. Preoperative demographics

Demographics	*Overall* *n = 4250*	*AKA* *n = 1941*	*BKA* *n = 2309*	P *value*
Age				.0001
50-59	19.3% (822)	15.7% (304)	22.4% (518)	
60-69	27.7% (1175)	25.8% (501)	29.2% (674)	
70-79	27.7% (1175)	27.5% (533)	27.8% (642)	
80-89	20.7% (879)	24.4% (474)	17.5% (405)	
90+	4.7% (199)	6.6% (129)	3.0% (70)	
Gender - male	59.3% (2521)	54.1% (1050)	63.7% (1471)	.0001
Race - white	59.1% (2512)	56.9% (1104)	61.0% (1408)	.007
Race - black	27.6% (1175)	31.2% (605)	24.7% (570)	.0001
Diabetes	62.4% (2652)	53.9% (1047)	69.5% (1605)	.0001
Smoking (within 1 year)	25.3% (1077)	26.4% (512)	24.5% (565)	.2
DNR status	7.4% (314)	11.1% (216)	4.2% (98)	.0001
Functional status				.0001
Independent	34.7% (1474)	24.6% (478)	43.1% (996)	
Partially dependent	46.1% (1958)	46.2% (897)	46.0% (1061)	
Fully dependent	19.3% (818)	29.2% (566)	10.9% (252)	
COPD	13.6% (579)	15.3% (297)	12.2% (282)	.004
CHF (within 30 days)	8.9% (377)	9.7% (188)	8.2% (189)	.09
MI (within 6 months)	6.1% (261)	6.4% (125)	5.9% (136)	.5
Percutaneous coronary intervention	16.2% (688)	14.9% (290)	17.2% (398)	.04
Prior cardiac surgery	27.5% (1167)	24.5% (476)	29.9% (691)	.0001
History of angina	2.5% (107)	2.5% (48)	2.6% (59)	.9
Hypertension	85.3% (3627)	84.5% (1641)	86.0% (1986)	.2
Prior revascularization or amputation for PVD	78.5% (3336)	75.4% (1464)	81.1% (1872)	.0001
Rest pain/gangrene	78.7% (3345)	78.7% (1527)	78.7% (1818)	1
Dialysis dependent	23.0% (976)	20.6% (399)	25.0% (577)	.0006
Stroke	25.5% (1083)	31.0% (601)	20.9% (482)	.0001
Open wound	75.2% (3197)	73.1% (1419)	77.0% (1778)	.003
Wound class				.4
Clean	42.2% (1795)	43.5% (845)	41.1% (950)	
Clean/contaminated	9.4% (399)	9.0% (174)	5.3% (225)	
Contaminated	20.5% (872)	20.1% (390)	20.9% (482)	
Dirty/infected	27.8% (1184)	27.4% (532)	28.2% (652)	
INR	1.28 ± 0.41	1.30 ± 0.44	1.26 ± 0.39	.0003
Serum creatinine	2.1 ± 2.0	1.9 ± 1.9	2.3 ± 2.1	.0001
Serum albumin	2.8 ± 0.7	2.7 ± 0.7	2.8 ± 0.7	.0001
White blood cell count	11.4 K ± 4.9 K	11.8 K ± 4.9 K	11.0 K ± 4.8 K	.0001
BMI	26.6 ± 6.8	25.6 ± 6.8	27.5 ± 6.7	.0001

AKA, Above-knee amputation; *BKA,* below-knee amputation; *BMI,* body mass index; *CHF,* congestive heart failure; *COPD,* chronic obstructive pulmonary; *DNR,* do not resuscitate; *INR,* international normalized ratio *MI,* myocardial infarction; *PVD,* peripheral arterial disease.

responsible for the statistical validity of the data analysis or the conclusions derived by the authors.

Study sample. The ACS-NSQIP database was queried by current procedural terminology (CPT) codes for transfemoral (CPT 27590 and 27591: above-knee amputation [AKA]) and transtibial amputations (CPT 27880 and 27881: below-knee amputation [BKA]) to produce the study sample. Excluded were patients having guillotine amputations and reamputations. De-identified data were obtained for patients that met these initial procedural criteria from January 1, 2005 through December 31, 2008 after local Institutional Review Board approval and additional permission from ACS-NSQIP (Chicago, Ill).

To maximize a study sample of patients requiring major amputation truly for CLI, the data was further restricted to only those with age 50 or greater and a history of ischemic rest pain or gangrene, or prior revascularization for peripheral vascular disease as part of their preoperative demographic data.

Outcome variables. The primary endpoint was defined as a wound occurrence within 30 days following major amputation. The specifically defined ACS-NSQIP wound occurrence outcomes included wound disruption, superficial incisional surgical site infection, and deep incisional surgical site infection. The secondary endpoint was 30-day mortality. Data from preoperative demographics, intraoperative variables, and 30-day follow-up were analyzed to identify independent predictors for the primary and secondary outcomes.

Statistical analysis. Baseline demographics (expressed as appropriate percents) and continuous variables (expressed as mean, ± standard deviation) were tabulated and subsequently studied with univariate analysis. χ^2 test of independence was used for categorical variables, and independent group's t test was used to analyze continuous measurements. Univariate comparisons with a P value of less than .05 were then studied with multiple logistic regression with odds ratios (OR) obtained for independent predictors. A P value equal to or less than .05 was considered to represent statistical significance.

Table II. Operative detail

Operative detail	*Overall* *n = 4250*	*AKA* *n = 1941*	*BKA* *n = 2309*	P *value*
Anesthesia - general	81.1% (3447)	82.7% (1605)	79.8% (1842)	.02
Anesthesia - spinal/epidural	15.1% (643)	14.2% (276)	15.9% (367)	.1
ASA class				.0001
I	0.1% (4)	0.00% (0)	0.2% (4)	
II	2.1% (399)	1.3% (26)	2.6% (61)	
III	55.4% (2353)	50.9% (988)	59.2% (1365)	
IV	42.4% (1801)	47.7% (926)	38.0% (875)	
Operative time (minutes)	66.2 ± 32.8	62.4 ± 33.0	69.4 ± 32.4	.0001

AKA, Above-knee amputation; *ASA,* American Society of Anesthesiologists; *BKA,* below-knee amputation.

Table III. Incidence of major postoperative occurrences

Postoperative occurrence	*Overall* *n = 4250*	*AKA* *N = 1941*	*BKA* *N = 2309*	P *value*
Superficial incisional infection	5.1% (215)	4.8% (94)	5.2% (121)	.6
Deep incisional infection	2.9% (125)	1.7% (33)	4.0% (92)	.0001
Dehiscence	1.7% (73)	1.3% (25)	2.1% (48)	.05
Death	9.6% (409)	12.0% (233)	7.6% (176)	.0001
Pneumonia	4.2% (180)	3.8% (74)	4.6% (106)	.2
Pulmonary embolism	0.59% (25)	0.72% (14)	0.48% (11)	.3
Renal insufficiency	0.92% (39)	0.88% (17)	0.95% (22)	.8
Stroke	0.92% (39)	1.29% (25)	0.61% (14)	.02
MI	0.89% (38)	0.77% (15)	1.00% (23)	.4
Deep venous thrombosis requiring therapy	0.59% (25)	0.57% (11)	0.61% (14)	.9

AKA, Above-knee amputation; *BKA,* below-knee amputation; *MI,* myocardial infarction.

RESULTS

There were 6592 patients identified in the NSQIP database that underwent major amputation between January 2005 and December 2008. Following exclusion criteria to maximize selection of CLI patients, 4250 had major amputation. Of those, 2309 patients underwent BKA and 1941 underwent AKA. Demographic and operation data for BKA and AKA groups are listed in Tables I and II, respectively. For the group as a whole, there were 78.5% that had a prior major amputation or prior revascularization for peripheral vascular disease, and there were 78.7% that had preoperative rest pain and/or gangrene. Major comorbidities for the study cohort included 62.4% with diabetes mellitus, 23.0% on hemodialysis, and 6.1% having had a myocardial infarction within 6 months. An open wound was present in 75.2% at the time of amputation.

For the study group as a whole, 5.1% developed superficial incisional infection, 2.9% developed deep incisional infection, and wound dehiscence occurred in 1.7% (Table III). BKA, compared with AKA, had significantly more deep incisional infection (4.0% and 2.1%, $P < .0001$) and wound dehiscence (1.7% and 1.3%, $P = .048$). Thirty-day mortality for the entire cohort was 9.6% with mortality after AKA (12%) being significantly higher ($P < .0001$) than BKA (7.5%). The incidence of postoperative stroke at 30 days was significantly higher ($P = .02$) in patients with AKA (1.29%) compared with BKA (0.61%).

By univariate analysis, there were significantly more wound occurrences ($P < .05$ for each parameter) for those patients who underwent a BKA in the 50 to 59 age group, for smokers within 1 year, for patients with a rising international normalized ratio (INR), and for patients with a lower preoperative creatinine (Table IV). Multivariate logistic regression analysis then determined that the 50 to 59 age group (OR = 1.9) and those with a higher INR (OR = 1.5) were significant predictors of a wound occurrence following BKA. Patients with higher preoperative creatinine were significantly less likely to have a wound occurrence (OR = 0.92) (Table V). The significant odds ratio of 1.5 for INR in this group meant that for every rise of 1 in the INR perioperatively, the risk of a wound occurrence increased by 1.5 times.

For patients who underwent an AKA, univariate analysis determined that smokers within one year, patients with a rising body mass index (BMI), and patients with an elevated white blood cell count had significantly more ($P <$ .05 for each parameter) wound occurrences (Table VI). Multivariate analysis determined smoking within one year and increasing BMI as significant predictors of a wound occurrence with odds ratios of 1.9 and 1.3, respectively (Table VII). For BMI, a patient was 1.3 times more likely to have a wound occurrence for every increase in BMI by 10 kg/m^2.

Thirty-day mortality was 7.6% for patients after BKA and 12% following AKA. There were numerous indicators for mortality following BKA and AKA (Tables VIII-XI). Significant independent predictors of mortality following BKA and AKA (Tables IX and XI) included congestive

Table IV. Univariate analysis on wound occurrences with BKA

Demographics	*n*	*Rate (%)*	P *value*
Age			
50-59 vs older	518	14.8	.003
60-69	674	10.5	
70-79	642	8.3	
80-89	405	8.6	
90+	70	7.1	
Gender			
Male	1471	10.2	.6
Female	838	10.9	
Race			
White	1408	10.9	.1
Black	570	8.3	
Other	331	12.1	
Anesthesia			
General	1842	10.7	.2
Epidural/spinal	367	15.9	
Other	100	4.3	
Diabetes	1605	9.9	.2
Non-diabetics	704	11.7	
Smoking			
Current within 1 year	565	13.1	.02
Non-smoker	1744	9.6	
DNR	98	9.2	.7
Full code	2211	95.8	
Functional status			
Dependent	252	10.3	1.0
Partially dependent	1061	10.7	
Independent	996	10.2	
COPD	282	9.2	.5
CHF (within 30 days)	189	11.6	0.6
MI (within 6 months)	136	10.3	1.0
Percutaneous coronary intervention	398	13.1	.06
Prior cardiac surgery	691	9.1	.2
History of angina (within 30 days)	59	17	.10
Hypertension	1986	10.2	.5
Dialysis dependent	577	8.8	.2
Stroke	482	10.8	.8
Open wound	1778	10.1	.3
ASA class			
I or II	65	12.3	.9
III	1365	10.3	
IV or V	875	10.5	
Wound class			
Clean	950	11.1	.6
Clean/contaminated	225	11.6	
Contaminated	482	10.4	
Dirty/infected	652	9.2	
Creatinine			.04
INR			.03
WBC			.6
Albumin			.5
BMI			1.0

ASA, American Society of Anesthesiologists; *BKA,* below-knee amputation; *BMI,* body mass index; *CHF,* congestive heart failure; *COPD,* chronic obstructive pulmonary; *DNR,* do not resuscitate; *INR,* international normalized ratio; *MI,* myocardial infarction; *WBC,* white blood cell count.

heart failure (OR = 1.7 and 2.3, respectively), chronic obstructive pulmonary disease (OR = 1.6 and 2.1), do not resuscitate status (OR = 3.1 and 2.0), functional status of fully dependent (OR = 2.2 and 2.5), and elevated white blood cell count (OR = 1.1 and 1.1). Additional significant predictors of mortality following BKA only included myocardial infarction within 6 months of amputation (OR = 1.8) and elevated creatinine (OR = 1.2), and an additional predictor of mortality following AKA only was requiring chronic hemodialysis preoperatively (OR = 2.1).

Table V. Multivariate analysis on wound occurrences with BKA

Predictor	*Odds ratio*	*95% Wald confidence limits*		P *value*
Age				
50-59 vs 60-69	1.5	1.04	2.17	.0024
50-59 vs 70-79	2.14	1.43	3.21	
50-59 vs 80-89	1.94	1.23	3.07	
50-59 vs 90+	2	0.77	5.21	
Serum creatinine	0.92	0.85	0.99	.0231
INR	1.46	1.1	1.93	.0089

BKA, Below-knee amputation; *INR,* international normalized ratio.

DISCUSSION

Despite great strides in limb salvage for CLI, major amputation remains a commonly performed operation on this debilitated group of patients. Not uncommonly, many of these patients have already endured a prolonged period of pain and suffering due to factors such as delays in diagnosis, failed revascularizations, interactions of comorbidities, and/or lack of healing despite optimal treatment. Therefore, a major amputation free from wound complications remains paramount to recovery and freeing the patient and family from continuous care surrounding the affected limb.

Utilizing the database of the National Surgical Quality Improvement Program, significant predictors of wound occurrences and mortality within 30 days have been identified for patients undergoing BKA and AKA for CLI. Over a 3-year period from 211 hospitals, 4350 patients underwent a major amputation that for CLI. Significant predictors of a wound occurrence following BKA included a younger age (50-59 years), lower preoperative creatinine, and an elevated INR at the time of operation. Significant predictors of a wound occurrence following an AKA included a smoking history and elevated BMI. These results further document in an objective way how distinctively different these two populations of patients are with the same disease (Table I). Moreover, these differences and predictors should give pause to formulating appropriate preoperative planning, postoperative and long-term care, and patient and family education. Lastly, initial presentation of rest pain, ischemic ulcer, or gangrene was not a predictor for a wound occurrence.

Younger patients (age group 50-59) were almost two times (OR 1.9) more prone to having a wound occurrence after BKA compared with their older age group comparators. Interestingly, advancing age with presumed increasing cardiovascular risk factors was not associated to increasing

Table VI. Univariate analysis on wound occurrences with AKA

Demographics	*n*	*Rate (%)*	P *value*
Age			
50-59 vs older	304	8.9	.3
60-69	501		
70-79	533		
80-89	474		
90+	129		
Gender			
Male	1050	6.8	.4
Female	891		
Race			
White	1104	7.2	.8
Black	605		
Other	232		
Anesthesia			
General	1605	7	.4
Epidural/spinal	276		
Other	60		
Diabetes	1047	7.2	.9
Non-diabetics	894		
Smoking			
Current within 1 year	512	10.4	.001
Non-smoker	1429		
DNR	216	4.2	.07
Full code	1725		
Functional status			
Dependent	566	5.7	.2
Partially dependent	897		
Independent	478		
COPD	297	6.1	.4
CHF (within 30 days)	188	8	.7
MI (within 6 months)	125	8	.7
Percutaneous coronary intervention	290	7.9	.6
Prior cardiac surgery	476	7.4	.9
History of angina (within 30 days)	48	4.2	.4
Hypertension	1641	7.6	.1
Dialysis dependent	399	6.8	.7
Stroke	601	6.5	.4
Open wound	1419	6.9	.4
ASA class			
I or II	26	7.6	.7
III	988		
IV or V	926		
Wound class			
Clean	845	5.5	.3
Clean/contaminated	174		
Contaminated	390		
Dirty/infected	532		
Creatinine			.2
INR			.5
WBC			.02
Albumin			.8
BMI			.04

AKA, Above-knee amputation; *ASA,* American Society of Anesthesiologists; *BMI,* body mass index; *CHF,* congestive heart failure; *COPD,* chronic obstructive pulmonary; *DNR,* do not resuscitate; *INR,* international normalized ratio; *MI,* myocardial infarction; *WBC,* white blood cell count.

wound occurrences. Explanations for increasing wound occurrences in this younger age group include having more aggressive atherosclerotic disease, subsequent early failure of revascularizations, and the combination of genetic predisposition, hypercoagulability, and virulent risk factors. The finding of increased wound occurrences in this younger age group could also be from additional different factors. These circumstances could include inappropriate delay in amputation from an overly aggressive desire to save the foot in a younger patient; inappropriate initial level of amputation with AKA perhaps being a better first choice for some patients; difficulties in care compliance in a more physically active age group; biased belief that this group of patients may not need the same skilled longer-term care and rehabilitation to heal a BKA compared with older counterparts. Nevertheless, it is this age group that may have the most to benefit from a BKA without wound complications. Attention to these details with respect to each patient's unique circumstances as well as perioperative normalization of the INR (with heparin transition if necessary) remains paramount to possibly avoiding these devastating complications and providing for return to earlier ambulation with a prosthetic limb.

Table VII. Multivariate analysis on wound occurrences with AKA

Predictor	*Odds ratio*	*95% Wald confidence limits*		P *value*
Smoking within 1 year				
Yes vs no	1.89	1.31	2.74	.0008
BMI	1.03	1.01	1.05	.0158

AKA, Above-knee amputation; *BMI,* body mass index.

While there was no difference in superficial incisional infection between BKA (5.2%) and AKA (4.8%), there were significant differences between the two types of amputation for deep incisional infection (4.0% vs 1.7%, respectively) and wound dehiscence (2.1% vs 1.3%, respectively). Possible explanations for these findings include AKA proximity to improved perfusion; BKA proximity to contaminated foot; and the ability of how each amputation incisional closure is able to accommodate a hematoma (ie, BKA being less tolerant of hematoma and therefore more susceptible to deep incisional infection and wound dehiscence).

In preventing wound occurrences following AKA, modifying the risk factors of increasing BMI (OR = 1.3) and smoking remain beyond the control of the surgeon. To further clarify regarding BMI, for every increase in the BMI of 10 kg/m^2, the risk of wound occurrence increases by another 30% (OR = 1.3). Certainly a meticulous attention to wound closure with every effort to sustain flap viability seems warranted. Appropriate choice and dosing of preoperative antibiotics with even higher intravenous loading doses than for patients with a normal BMI may help prevention wound infection in this debilitated population.

There is a paucity of scientific literature reporting outcomes following major amputation in patients with CLI, particularly with regards to wound problems and infection. Sadat et al concluded that a 5-day course of antibiotics significantly reduced wound infection rates and hospital

Table VIII. Univariate analysis on death with BKA

Demographics	*n*	*Rate (%)*	P *value*
Age			
50-59 vs older	518	4.3	<.0001
60-69	674	5.8	
70-79	642	9.4	
80-89	405	10.9	
90+	70	15.7	
Gender			
Male	1471	8.1	.3
Female	838	6.8	
Race			
White	1408	8.2	.4
Black	570	6.8	
Other	331	6.3	
Anesthesia			
General	1842	7.2	.3
Epidural/spinal	367	9.3	
Other	100	10	
Diabetes	1605	7.0	.1
Non-diabetics	704	9.0	
Smoking			
Current within 1 year	565	5.0	.01
Non-smoker	1744	8.5	
DNR	98	25.5	<.0001
Full code	2211	6.8	
Functional status			
Dependent	252	13.5	<.0001
Partially dependent	1061	9.3	
Independent	996	4.3	
COPD	282	13.1	.0002
CHF (within 30 days)	189	16.4	<.0001
MI (within 6 months)	136	14.7	.001
Percutaneous coronary intervention	398	7.8	.9
Prior cardiac surgery	691	9.4	.04
History of angina (within 30 days)	59	13.6	.08
Hypertension	1986	7.6	.8
Dialysis dependent	577	13.9	<.0001
Stroke	482	7.9	.8
Open wound	1778	7.8	.5
ASA class			
I or II	65	4.6	<.0001
III	1365	5.1	
IV or V	875	11.8	
Wound class			
Clean	950	6.7	.2
Clean/contaminated	225	10.7	
Contaminated	482	6.9	
Dirty/infected	652	8.4	
Creatinine			<.0001
INR			.05
WBC			.002
Albumin			.0003
BMI			.009

ASA, American Society of Anesthesiologists; *BKA,* below-knee amputation; *BMI,* body mass index; *CHF,* congestive heart failure; *COPD,* chronic obstructive pulmonary; *DNR,* do not resuscitate; *INR,* international normalized ratio; *MI,* myocardial infarction; *WBC,* white blood cell count.

Table IX. Multivariate analysis on death with BKA

Predictor	*Odds ratio*	*95% Wald confidence limits*		P *value*
Age				
60-69 vs 50-59	1.2	0.69	2.11	.0219
70-79 vs 50-59	1.86	1.09	3.19	
80-89 vs 50-59	2.22	1.24	3.98	
90+ vs 50-59	2.63	1.07	6.48	
DNR				
Yes vs no	3.13	1.81	5.42	.0001
Functional status				
Partially dependent vs independent	1.61	1.09	2.38	.0074
Totally dependent vs independent	2.19	1.31	3.66	
COPD				
Yes vs no	1.58	1.02	2.44	.0392
CHF				
Yes vs no	1.72	1.07	2.78	.0265
MI (within 6 months)				
Yes vs no	1.82	1.04	3.19	.0347
BMI	0.97	0.95	1	.0497
Serum creatinine	1.24	1.16	1.33	.0001
White blood cell count	1.057	1.026	1.089	.0003
Platelet count	0.997	0.996	0.999	.0001
Total op time (minutes)	0.993	0.987	1	.0352

BMI, Body mass index; *CHF,* congestive heart failure; *COPD,* chronic obstructive pulmonary; *DNR,* do not resuscitate; *MI,* myocardial infarction.

length of stay in this population.[9] In this historical case-control study of two similar groups of 40 consecutive major amputations, the group receiving the 5-day antibiotic regimen had a significantly lower infection rate compared with the 24-hour antibiotic regimen group (5% vs 22.5%, $P = .023$). While a 5-day course of prophylactic antibiotics remains controversial, Hall et al found similar reductions in infection rates in a prospective randomized study of 302 patients undergoing vascular reconstructions.[10] This study's multidose antibiotic group (mean treatment of 3 days) had significantly less wound infection compared to the single-dose group (10% vs 18%, $P = .04$). The NSQIP database does not provide information regarding use of prophylactic antibiotics. Nevertheless, other programs such as the Surgical Care Improvement Project (SCIP) have moved hospitals into compliance in assuring single dose antibiotics are given within one hour of incision. Given the preliminary data from the aforementioned studies of the beneficial effects of continued prophylactic antibiotics after a major amputation, and the contrast to SCIP recommendations of one-time antibiotic dosing just prior to operation, the "one size" fits all concept may not be applicable to certain operations such as major amputation for patients with CLI. Hence, a well-designed randomized double-blind placebo controlled trial examining optimal prophylactic antibiotic treatment timing could address this important issue in patients undergoing major amputation. The NSQIP data presented herein on wound occurrences following major amputation for CLI represents the first on a large-scale from a quality driven validated program and database.

Wound occurrence, defined as wound disruption, superficial incisional surgical site infection, and deep incisional surgical site infection was defined as the primary

Table X. Univariate analysis on death with AKA

Demographics	*n*	*Rate (%)*	P *value*
Age			
50-59 vs older	304	8.6	.0007
60-69	501		
70-79	533		
80-89	474		
90+	129		
Gender			
Male	1050	11.1	.2
Female	891		
Race			
White	1104	13.4	.09
Black	605		
Other	232		
Anesthesia			
General	1605	12.3	.6
Epidural/spinal	276		
Other	60		
Diabetes	1047	12.2	.8
Non-diabetics	894		
Smoking			
Current within 1 year	512	7.8	.0007
Non-smoker	1429		
DNR	216	21.3	.0001
Full code	1725		
Functional status			
Dependent	566	20.3	.0001
Partially dependent	897		
Independent	478		
COPD	297	18.9	.0001
CHF (within 30 days)	188	26.1	.0001
MI (within 6 months)	125	17.6	.05
Percutaneous coronary intervention	290	13.5	.4
Prior cardiac surgery	476	13	.4
History of angina (within 30 days)	48	14.6	.6
Hypertension	1641	11.9	.7
Dialysis dependent	399	19.1	<.0001
Stroke	601	11.8	.9
Open wound	1419	11.3	.1
ASA class			
I or II	26	16.4	<.0001
III	988		
IV or V	926		
Wound class			
Clean	845	11.3	.09
Clean/contaminated	174		
Contaminated	390		
Dirty/infected	532		
Creatinine			.002
INR			.02
WBC			.003
Albumin			.0001
BMI			.1

AKA, Above-knee amputation; *ASA,* American Society of Anesthesiologists; *BMI,* body mass index; *CHF,* congestive heart failure; *COPD,* chronic obstructive pulmonary; *DNR,* do not resuscitate; *INR,* international normalized ratio; *MI,* myocardial infarction; *WBC,* white blood cell count.

Table XI. Multivariate analysis on death with AKA

Predictor	*Odds ratio*	*95% Wald confidence limits*		P *value*
Age				
60-69 vs 50-59	1.13	0.65	1.97	.005
70-79 vs 50-59	1.21	0.71	2.07	
80-89 vs 50-59	1.74	1.01	2.97	
90+ vs 50-59	3.09	1.56	6.13	
DNR				
Yes vs no	2.01	1.32	3.07	.0013
Functional status				
Partially dependent vs independent	1.1	0.69	1.74	.0001
Totally dependent vs independent	2.47	1.56	3.9	
COPD				
Yes vs no	2.08	1.43	3.03	.0001
CHF				
Yes vs no	2.26	1.5	3.39	.0001
Dialysis				
Yes vs no	2.44	1.72	3.47	.0001
White blood cell count	1.057	1.025	1.09	.0004
Platelet count	0.996	0.995	0.998	.0001

AKA, Above-knee amputation; *CHF,* congestive heart failure; *COPD,* chronic obstructive pulmonary; *DNR,* do not resuscitate.

endpoint in this study and determined to be 9.7%. Other studies have documented high rates of infection following major amputation. Van Niekerk determined in a prospective cohort (n = 234 amputations for peripheral arterial disease [PAD] or diabetes mellitus) a stump infection rate of 42% for AKAs and 23% for BKAs. The study also determined that patients who had a previous bypass procedure had a significantly higher level of major amputation as well as stump infection.[11] Another study by Taylor et al determined in defining a successful outcome for BKAs that the healing rate without the need for revision was 86.4%.[12] Similarly, Lim et al reported in a retrospective study of 87 patients a wound infection rate of 29.4% for BKAs, 22.6% for AKAs, and a revision rate of 17.6%.[13] The study presented herein using NSQIP data does not have information as to the number of revisions that were performed as linked to each particular patient, particularly those patients subsequently requiring an AKA after a previous BKA. Whereas the need for operative revision remains an important factor in recovery, it is the wound occurrence that leads to the need for revision. Determining those significant factors that contribute to a wound dehiscence or infection can help in prevention of higher level amputation for future patients.

There are a number of severe comorbid conditions that are significantly associated with the 7.6% 30-day mortality following BKA and 12% following AKA (Tables IX and XI). Previous reports from smaller studies report a range of 30-day mortality following BKA of 4.2% to 12% and following AKA of 13.5% to 17.8%. Not unexpectedly, 1-year survival rates are poor in patients undergoing major amputation with CLI and range from 49.6% to 80.4%.[6,7,14-23] Knowing what cormorbidities are more likely to contribute to death following major amputation may temper the aggressiveness to amputate in certain circumstances. Not uncommonly, these patients harbor multiple severe comorbidities, have limited or no ambulation capability, and are toward the end of life. Major amputation may be more appropriate only in certain circumstances such as if ischemic pain is severe and cannot be controlled, uncontrolled infection is present, or the wound on the lower leg or foot cannot receive adequate care.

Knowing the risks of mortality after major amputation remains vitally important in communicating to patients, families, consultants, and primary care physicians. For example, when using those significantly associated comorbid conditions to predict the probability of mortality following BKA in the 80- to 89-year-old patient, the risk of death can vary from 0.35% to 78% depending on the combination status of do not resuscitate, function/dependency, chronic obstructive pulmonary disease, myocardial infarction, and renal function. When these conditions are at their lower level, mortality is very high. Hence, depending on the patient and the severity of CLI, amputation may not be the best choice in some patients compared with good supportive care. Clearly, for patients with multiple serious comorbid conditions, the indication for major amputation may relate more to pain status, infection status, and ease of wound care.

Use of the NSQIP database presents several limitations that have been previously cited.[24,25] Because of the large sample size, some comparisons can demonstrate a highly significant difference, but not be as clinically relevant. The qualifications of the general or vascular surgeons performing the procedures are unknown. Additionally, the operative technique as well as the postoperative care can be variable per independent surgeon preference. The NSQIP database does not include all consecutive surgical patients nor the intention to treat. By using a methodical sampling system, the hope is to portray meaningful outcomes when the data is taken in aggregate and tracked over time. Furthermore, the primary purpose of the NSQIP is to improve quality as each hospital uses the same sampling method and then can observe their outcome of each measure compared to other hospitals.

CONCLUSIONS

Wound occurrences continue to be a serious problem in patients undergoing major amputation for CLI. Using the NSQIP database, certain clinical factors significantly increase those risks, thus leading to prolonged suffering and delay in recovery. For BKA, elevated INR and being in the 50 to 59 age group proved to be predictive, and, for AKA, the predictive factors were current smoking history and obesity. Whether the patient is a previously ambulatory 50-year-old or nonambulatory 85-year-old, working towards proper surgical healing to minimize wound occurrence at every clinical level can make a substantial difference for the patient and the multifaceted care team.

AUTHOR CONTRIBUTIONS

Conception and design: RH, RM, CM, DH, DR, KH
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Data collection: RH, RM
Writing the article: RH, RM
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Final approval of the article: RH, RM, CM, DH, DR, KH
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